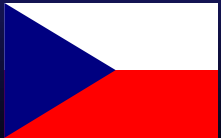




BW THREAT REDUCTION MEDICAL PROPHYLAXIS IN THE CZECH REPUBLIC

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AIM OF THE PRESENTATION

- **Medical response to BW threat**
- **Preexposure and postexposure medical prophylaxis**
- **Czech vaccination policy**





Medical Response to BW Threat





BW threat

Who are 1st Responders?

- **Primary Care Personnel**
- **Hospital Staff**
- **EMS Personnel**
- **Public Health Professionals**
- **Other Emergency Preparedness Personnel**
- **Laboratory Personnel**
- **Law Enforcement**





MEDICAL RESPONSE

- **Pre - exposure period**
 - surveillance system (to monitor unusual illnesses or outbreaks of disease)
 - detection, identification of threat / use
 - chemoprophylaxis
 - immunization
 - education

Diference must be made between

- detection of biological agents in the environment (detection, monitoring)
- medical diagnostics (detection of B- agents, components of agents, or antibodies to B-agents in tissue samples – blood,body fluids)





MEDICAL RESPONSE

- **Post – exposure period**
 - incubation period
 - active and pasive immunization
 - antimicrobial or supportive therapy
 - isolation precaution
 - observation, quarantine, ROM
 - disease onset period
 - diagnosis
 - treatment
 - direct patient care





Pre-exposure and Post-exposure Medical Prophylaxis

**The main goal:
Minimize potential impact of BW**





PRE-EXPOSURE MEDICAL PROPHYLAXIS

- **Immunoprophylaxis**
 - vaccines against a number of potential BW agents are available
 - many of these vaccines were developed for the protection of laboratory workers or individuals in endemic areas
 - vaccines which are effective under natural circumstances, may not provide a similar degree of protection to people exposed to BA attack
 - vaccines do not immediate protection
- **Chemoprophylaxis**
 - using appropriate drugs offers additional protection
 - must be available for all personel in BW area









POST-EXPOSURE MEDICAL PROPHYLAXIS

- **Chemoprophylaxis**
 - anthrax (for 60 days)
 - Ciprofloxacin 500 mg PO 2x a day
 - Doxycycline 100 mg PO 2x a day
 - Amoxycilin 500 mg PO 2x a day
 - plaque (7 days)
 - Doxycycline 100 mg PO 2x a day
 - Ciprofloxacin 500 mg PO 2x a day
 - Tularemia (14 days) – Gentamicin, Ciprofloxacin
 - Cholera (7 days)
 - Brucellosis (3 weeks) – ?? Rifampicin, Doxycycline
 - VHF: Ebola, Lassa
 - antivirotics Ribavirin





POST-EXPOSURE MEDICAL PROPHYLAXIS

- **Active and passive immunization**
 - **vaccines exist against**
 - anthrax
 - smallpox
 - plaque – a killed whole-cell vaccine (pneumonic form ?)
 - tularemia – as investigational new drug in US
 - cholera – DUKORAL, oral live attenuated vaccine, 1 dose
 - Q fever – Q-VAX, formalin killed *C. burnetii*, 1 dose, 5 Y protection
 - VEE – live attenuated vaccine (experimental TC – 83)
 - WEE, EEE – inactivated vaccines
 - botulism – pentavalent toxoid of *C. botulinum* types A,B,C,D,E
 - **vaccines don't exist against**
 - brucellosis, VHF (except Yellow fever), AHF – under development, Ricin, Saxitoxin





SMALLPOX VACCINATION

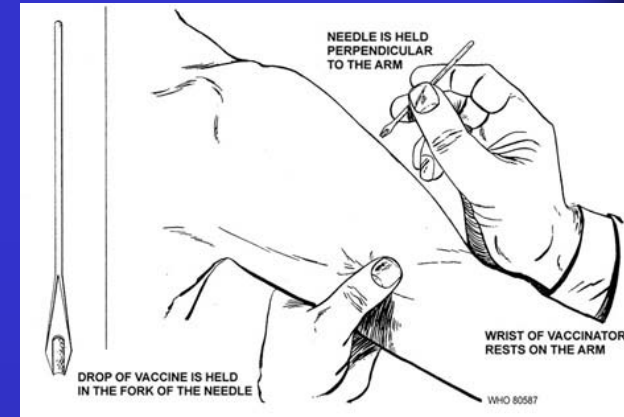
- Different vaccinia strains have been used for production of vaccine
 - New York City Board of Health (NYCBOH) for US vaccine
 - Dryvax; Aventis Pasteur vaccine
 - newly developed ACAM 1000 (human embryonic lung cell culture) and ACAM 2000 (African green monkey cells – vero cells)
 - live lyophilised Czech vaccine – VARIE + solution VARISOL
 - vaccinia strain used to infect heifer's skin
 - old vaccine from the 1980's





VACCINATION

- Intradermal inoculation with bifurcated needle (scarification)
- Vaccinia virus replicates in the dermis of the skin
 - “Major reaction”-
 - Pustular lesion or area of induration surrounding a central lesion (scab or ulcer) 6-8 days after primary vaccination
 - can be misdiagnosed as bacterial superinfection
 - Low grade fever, axillary lymphadenopathy
 - Scar constitutes permanent record of successful vaccination





Primary Vaccination Site Reaction

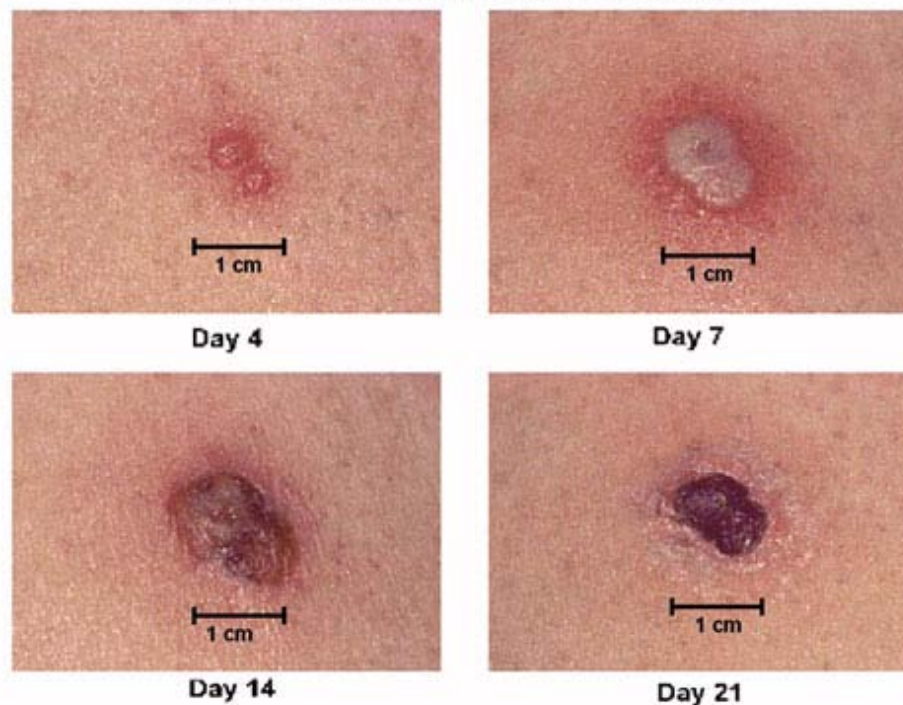


FIGURE 4. Example of a major reaction (i.e., a take) in a first-time smallpox vaccinee at 6 (left), 10 (middle), and 15 (right) days postvaccination



Source: Reproduced with permission of Stephen P. Heyse, M.D., National Institutes of Health.

Note: Vaccination reactions in vaccinia-naïve and previously vaccinated volunteers in a clinical study of diluted Dryvax[®] smallpox vaccine; volunteers were enrolled at the NIAID-supported Vaccine Treatment and Evaluation Unit at Saint Louis University in 2002.





VACCINIA CONTACT PRECAUTIONS

- **Vaccinia present at lesion from papule (2-5 d) until scabbed (10-19 d p vaccination)**
 - lesion covered by dry semipermeable dressing
 - transparent dressings predispose to local secondary inoculation
 - strict handwashing after dressing change
- **Vaccinia can be transmitted from a vaccinee's unhealed vaccination site**
 - by close contact
 - can lead to the same adverse events as in the vaccinee
- **Excluded from care of vaccinia lesions if pregnant, immunocompromised, or with chronic exfoliative dermatoses**





ADVERSE EVENTS

- The frequencies were identified in studies of the 1960s.
- Unknown prevalence of risk factors among today`s population
- Precise predictions of adverse reaction rates are unavailable
- Range from mild and self-limited to severe and life-threatening





VACCINIA-COMPLICATIONS

- Normal host
 - Inadvertent inoculation (skin, eye)
 - Generalized vaccinia
 - E. multiforme, urticarial eruptions
 - Postvaccinal encephalopathy, encephalomyelitis
- Pregnancy
 - Fetal vaccinia
- Eczema/exfoliative dermatoses/burns
 - Eczema vaccinatum
- Immunocompromised
 - Vaccinia necrosum





Complication Rates-Vaccinia (Cases per million vaccines)*

<u>Complication Rate</u>		<u>Complication Rate</u>	
Inadvertent inn.	42	V. necrosum	3
E. multiforme	10	Encephalitis	2
Generalized vacc	9	Other**	39
E. vaccinatum	3	Total	108

* Adapted from Lane et al., *J Infect Dis* 1970;122:303-309

** Incl. bacterial superinfections and lesions uncomfortable enough to result in physician contact. Unusual complications incl. fetal vaccinia, melanoma at vaccine scar, and monoarticular arthritis





FIGURE 20. Generalized vaccinia with a substantial erythematous base in an infant; note the vaccination site at the left axilla and the apparently well child



Source: Reproduced with permission of J. Michael Lane, M.D.



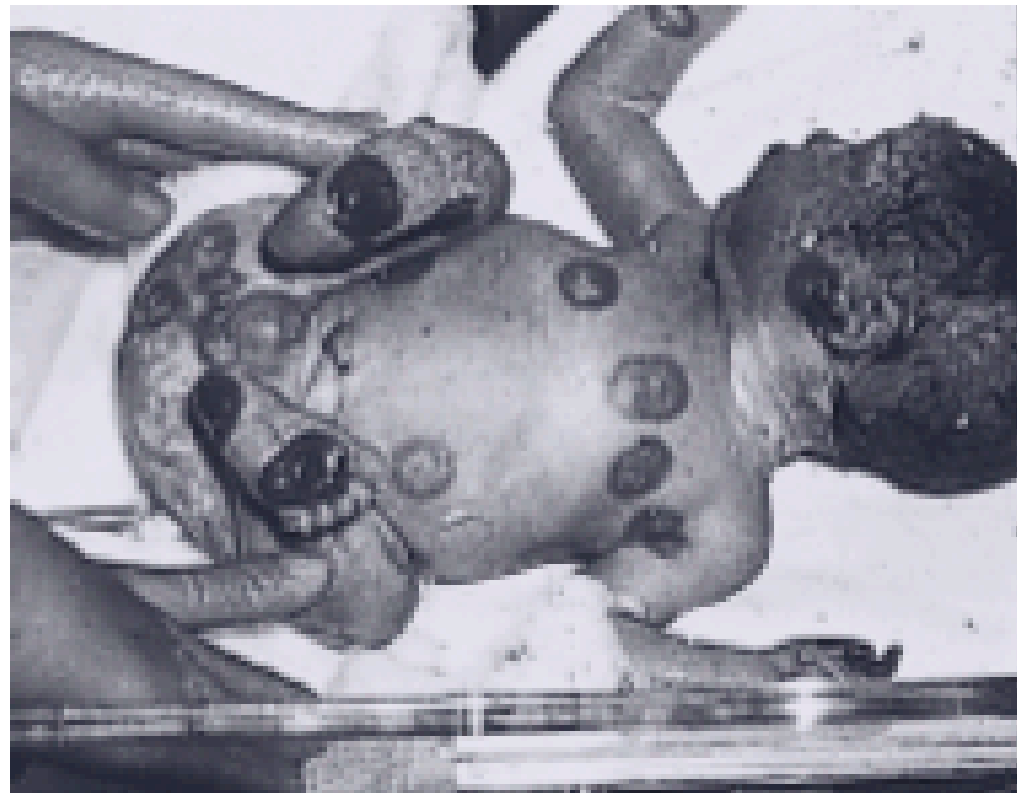
FIGURE 24. (Top left) A woman aged 22 years with eczema vaccinaria acquired from a close contact. She became critically ill, with nearly total involvement of her body, and required thiosemicarbazones, as well as substantial doses of vaccinia immune globulin; (right) side view; (bottom left) residual scarring after resolution of systemic illness



Source: Reproduced with permission of J. Michael Lane, M.D.



FIGURE 33. Fetal vaccinia in a premature infant, 28 week's gestation. Mother received vaccination at 23 week's gestation. The infant died at age 8 days, and vaccinia was isolated from the placenta



Source: Reproduced with permission of J. Michael Lane, M.D.



VACCINE CONTRAINDICATIONS

- **Immunosuppression**
 - autoimmune condition, cancer, radiation treatment, immunosuppressive medications
- **HIV infection**
- **History or evidence of eczema**
 - possibly other exfoliative or extensive skin lesions-psoriasis, burns
- **Pregnancy**
- **Household/close contacts with above**
 - There were no contraindications to vaccinating contacts during era of endemic smallpox





Vaccinia Immune Globulin (VIG)

- Sterile solution of the Ig fraction of plasma with antibodies to vaccinia virus from vaccinated persons
- Must be available to give vaccinia safely, efficacy in the treatment of adverse reactions
- Dose: 0.6 ml/kg IM (can be given at multiple sites/divided doses over 24 -36 hrs)
- VIG administration is not without risk
- VIG is not recommended for prophylaxis of persons with Smallpox vacc. contraindications
- In Development:
 - IV product
 - Humanized monoclonal antibodies vs epitopes conserved between variola and vaccinia





SMALLPOX: MANAGEMENT OF CONTACTS

- Immediate vaccination (or boosting) of all potential contacts incl. HCWs
 - Clinical “take” within three years confers immunity
 - Most effective if given < 24 hrs p exposure
 - Given within 1 week of exposure can prevent or attenuate disease
- Pregnancy, dermatoses
 - Vaccine + VIG Vaccinia immune globulin (VIG) 0.6 ml/kg IM
 - VIG given using multiple doses/sites/24-36 hrs
- Immunocompromised
 - VIG





CHEMOPROPHYLAXIS

- Chemoprophylaxis no longer available
- Methisazone (Marboran, Burroughs Wellcome)
 - Decreased morbidity and mortality when given to susceptible contacts
 - Limiting side effects: GI intolerance
 - No longer manufactured-not available
- Cidofovir
 - Active in vitro vs variola
 - Active in vivo: postexposure prophylaxis, monkeypox model (rhesus macaques)





Czech Vaccination Policy





CZECH VACCINATION POLICY

- **Civilian and military stockpile of Smallpox vaccines**
- **Only military stockpile of Anthrax vaccines**
- **Smallpox vaccination - when and who?**
 - only in case of infection apparation as postexposure vaccination
 - for civilian and military people
- **Anthrax vaccination – when and who?**
 - before unit deployment in risk areas (abroad mission)
 - only military personal





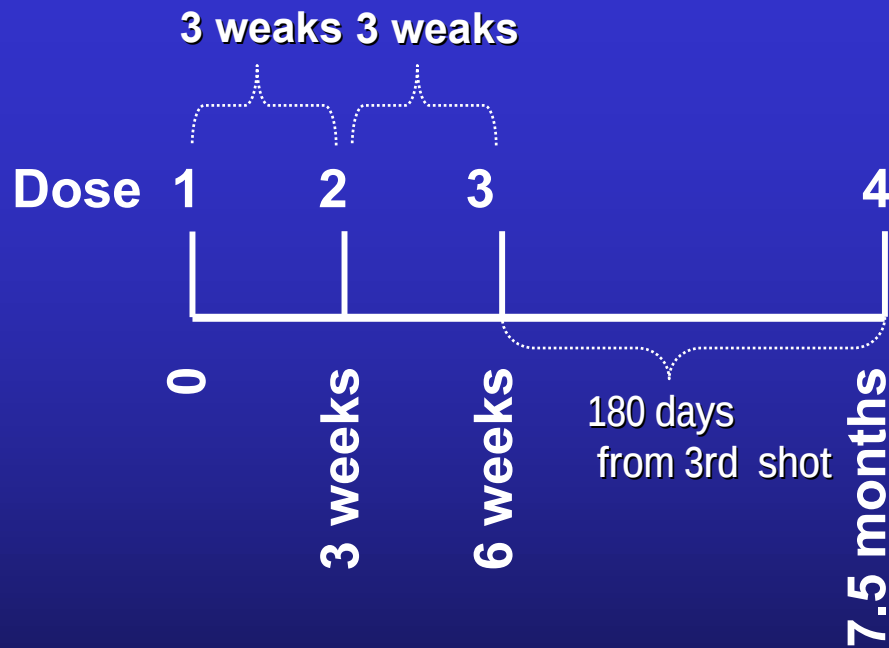
ANTHRAX VACCINATION IN THE CZECH ARMY

- **Anthrax Vaccine**
 - produced by MRA/CAMR, Porton Down, Salisbury, UK
 - anthrax antigen + potassium – aluminium sulphate, thiomersal, sodium chlorid, aqua
- **Volume: 0.5 ml**
- **Administration: i.m.**
- **Booster: 0.5 ml every year**





CZECH VACCINE SCHEDULE

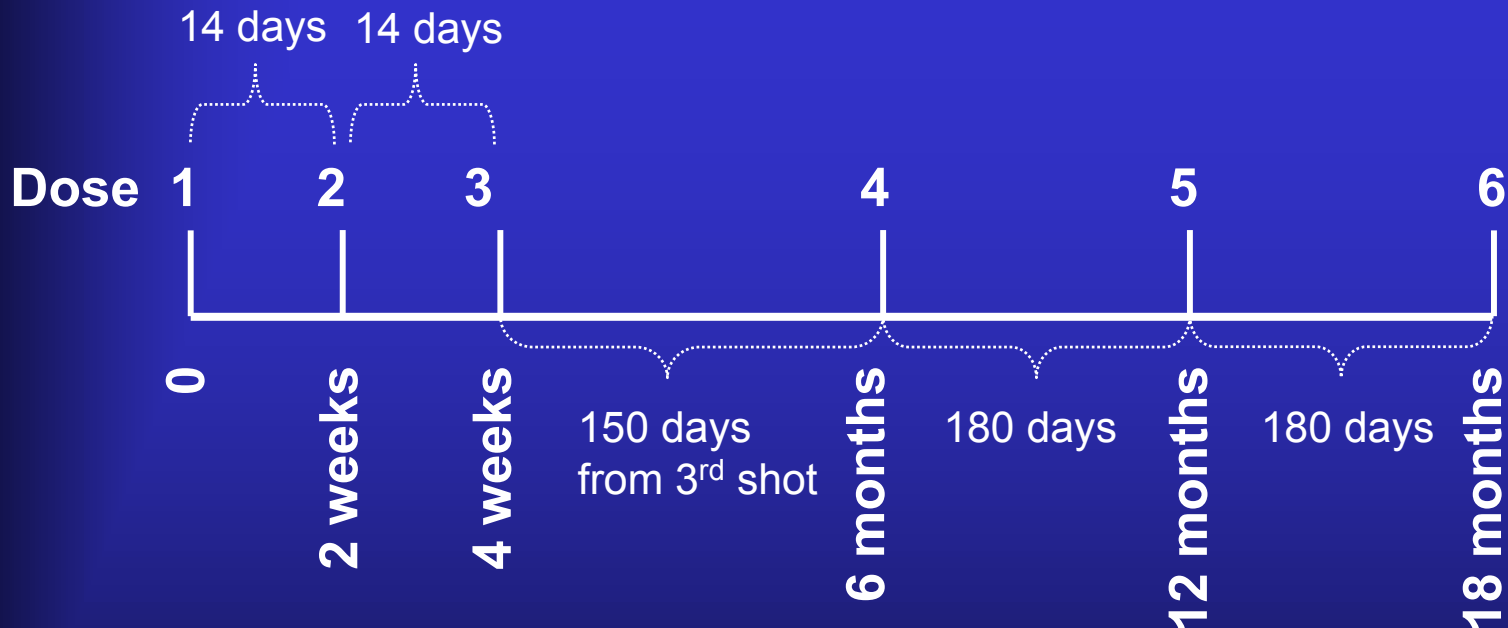


- **Four shots over 7.5 months, plus annual boosters**





US Vaccine Schedule



- Six shots over 18 months, plus annual boosters
- Do not compress the schedule
- Adjust schedule for individual delays





ADVERSE REACTIONS

- **Approx. 353 vaccinees; 4 refused vaccination**
- **No clinical trial, only approximated data**
 - local reactions – the most common reactions – pain, redness
 - systematic reactions – headache, myalgia, arthralgia, fatigue, fever up to 38° C
- **25 vaccinees found medical advice**
 - 8 vaccinees had operating incapacity
- **Persisting for 3-4 days**
- **Anaphylaxis reaction was not reported**





SUMMARY

- **Medical prophylaxis** can minimize impact of BW threats
- **Vaccination** is the only practical means of providing continuous protection against BW threats prior to, as well as during, hostile actions
- Initiation of **chemoprophylaxis** during the incubation period is always helpful however the earlier the ATB is given the greater is the change of preventing disease
- The **combined use** of medical countermeasures, physical protection, warning, detection and hazard management provides the basis of defence





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